<Division of Synthetic Chemistry> Synthetic Organic Chemistry

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- Synthetic Organic Chemistry -

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Visitors

Prof CLAYDEN, Jonathan — Department of Chemistry, University of Manchester, England, 26 March, 2004
Prof KAGAN, Henri Boris — Institut de Chimie Molculaire et des Materiaux, Universite de Paris-Sud, France, 18 - 19 November, 2004

Scope of Research

The research interests of the laboratory include the development of new synthetic methodology, total synthesis of biologically active products, and molecular recognition. Programs are active in the areas of asymmetric alkylation of carbonyl compounds based on "memory of chirality", nucleophilic catalysis for selective reactions, synthesis of unusual amino acids and nitrogen heterocycles, visualization of molecular chirality by functionalized phenolphthalein, use of homooxacalixarene for molecular recognition, and the structural and functional investigation of heterochiral oligomers.

Research Activities (Year 2004)

Presentations

Asymmetric Synthesis of Cyclic Amino Acids via Memory of Chirality, KAWABATA T, IUPAC International Conference on Biodiversity and Natural Products: Chemistry and Medicinal Applications, 31 January.

Asymmetric Synthesis of Cyclic Amino Acids via Enolates with Dynamic Chirality, KAWABATA T, 7th International Symposium on Carbanion Chemistry, 11 July.

Preparation and Properties of C_2-Symmetric Chiral PPY Analogues, SCHEDEL H, KAWABATA T, 15th International Conference on Organic Synthesis (IUPAC ICOS-15), 5 August.

Asymmetric Synthesis of Nitrogen-Containing Heterocycles via Memory of Chirality, KAWABATA T, MAJUMDAR S, KAWAKAMI S, The 14th International Symposium on Fine Chemistry and Functional Polymer, 18 August.

Construction of Variable Temperature Visual Read Out System for Sodium and Potassium Ions, TSUBAKI K, TANIMA D, KAWABATA T, International Conference on Supramolecular Science & Technology 2004, 9 September.

An Artificial Potassium Ionophore Based on D,L-Oligoester Architecture, KAWABATA T, OKAZAKI A, HIGASHINO I, 30th Symposium on Progress in Organic Reactions and Synthesis, Japan, 20 October.

Grants

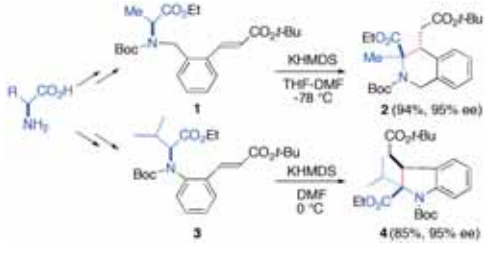
Kawabata T, Design of a New Generation of Nucleophilic Catalysts and Selective Reactions, Grant-in-Aid for Scientific Research (B) (2), 1 April 2002 - 31 March 2005.

Kawabata T, Development of C_2-Symmetric Chiral Nucleophilic Catalysts and Use in Asymmetric C-C Bond Formation, Grant-in-Aid for Scientific Research, 25 June 2004 - 24 June 2006.

Kawabata T, Asymmetric Cyclization based on the

A Novel Route to Highly Substituted Nitrogen Heterocycles from α-Amino Acids

Nitrogen-containing heterocycles constitute important pharmacophore for drug discovery, useful building blocks for natural product syntheses, and the key structural subunits in asymmetric catalysis. We developed a novel route to highly substituted nitrogen heterocycles from readily available α-amino acids. Treatment of **1** with potassium hexamethyldisilazide (KHMDS) at –78°C gave tetrahydroisoquinoline derivative **2** as a single diastereomer in 95% ee. Similarly, on treatment of **3** with KHMDS at 0°C gave indoline derivative **4** in 95% ee. Chirality of the parent amino acid derivatives was preserved during the enolate-formation and the subsequent conjugate addition process. Thus, asymmetric synthesis was accomplished in the absence of external chiral sources such as chiral catalysts. This method is applicable to the synthesis of various nitrogen heterocycles with contiguous quaternary and tertiary stereocenters.



An Artificial Potassium Ionophore Based on D,L-Oligoester Architecture

Homochiral oligoesters such as an oligolactate preferentially form a helical structure. On the other hand, D,L-oligolactate, consisting of alternating D- and L-lactic acid, favorably adopt a higher-ordered cyclic structure when lactic units are in the range of 6~8. Structural analysis indicated that the cyclic structure of these D,L-oligolactate is not the result from intramolecular hydrogen-bonding, but from their D,L-chirality. Ion-transport experiments were performed with octaesters **5** and **6** consisting of 2-hydroxy-3-phenylpropionic units. D,L-Octaester **6** showed the higher rate of ion transport both for Na^+ and K^+ than the corresponding homochiral octaester **5**. Potassium ion was selectively transported by **6** and the rate was much higher than that by dibenzo 18-crown-6 and comparable with that of sodium-ion transport by a well-known ionophore, monensin. These properties of **6** seem to originate from its cyclic preorganized structure **A**.

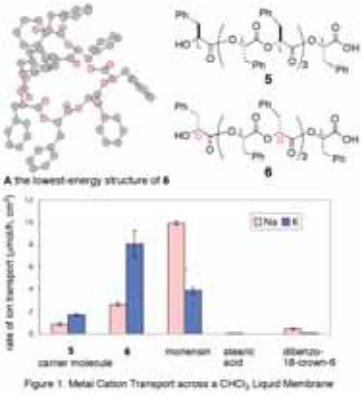
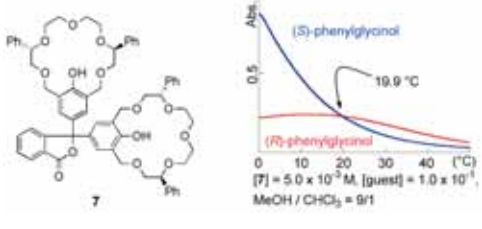


Figure 1. Metal Cation Transport across a $CHCl_3$ Liquid Membrane

Temperature-Dependent Visual Enantiomeric Recognition of β-Amino Alcohols

Optically active artificial host molecule 7 consisting of a phenolphthalein skeleton and two crown ethers has been prepared and used for visual enantiomeric recognition of β-amino alcohols in a protic media. A wide range of (*S*)-β-amino alcohols induced deeper coloration in 7 than the corresponding (*R*)-β-amino alcohols at 0°C. The absorbance inversion temperatures (*AITs*) were observed within the range of 0 to 50°C in the several cases. For example, the absorption between 7 and (*S*)-phenylglycinol is stronger than that with (*R*)-form below 19.9°C. On the other hand, color development with 7 and (*R*)-phenylglycinol is deeper above this temperature. This is one of the very few examples where AIT is observed in a diastereomeric host-guest interaction.



Dynamic Chirality of Enolates, Grant-in-Aid for Scientific Research, 31 October 2002 - 30 October 2004.

Awards

TSUBAKI Kazunori, The Society of Synthetic Organic Chemistry, Japan, Kansai Branch Award, 19 November 2004.

MONGUCHI Daiki, Best Poster Award, 21st Summer School of Synthetic Organic Chemistry, 14 July 2004.